LISTING OF CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1 – 20. (Cancelled)

21. (Previously presented) A method for determining the presence, amount, or activity of one or more active target proteins in a complex protein mixture, the method consisting essentially of:

(a) contacting said complex protein mixture with a single activity based probe that specifically binds predominantly to a single target site on one or more active target proteins;

(b) optionally binding said target protein(s) to a solid support;

(c) proteolyzing said active target protein(s) to produce a product mixture;

(d) separating said product mixture into two or more components, one or more of which consist essentially of peptides bound to said probe; and

(e) generating a signal from said peptides bound to said probe, wherein said signal is correlated to the presence, amount, or activity of said one or more active target proteins in said complex protein mixture.

22. (Previously presented) A method according to claim 21, wherein said separating step (d) consists essentially of sequestering one or more peptides bound to said probe using a receptor that specifically binds to said probe.

23. (Previously presented) A method according to claim 22, wherein said probe consists essentially of a functional group, a detectable label, an optional affinity group, and an optional linking group, and said receptor is an antibody or fragment thereof that binds to said detectable label.

24. (Previously presented) A method according to claim 23, wherein said detectable label consists essentially of a fluorescent moiety, and said signal is a fluorescent signal generated from said probe.

25. (Original) A method according to claim 21, wherein said signal is a mass spectrum.

26. (Previously presented) A method according to claim 21, wherein, prior to said proteolyzing step (c), one or more components of said complex protein mixture not bound to said probe are removed from said complex protein mixture.

27. (Previously presented) A method according to claim 21, wherein said probe consists essentially of a functional group, a detectable label, an optional affinity group, and an optional linking group, and said detectable label is selected from the group consisting of a fluorescent moiety and an isotopic label.

28. (Previously presented) A method according to claim 21, wherein said separating step (d) is selected from the group consisting of affinity separation, gel electrophoresis, capillary electrophoresis, liquid chromatography, HPLC, electrospray ionization mass spectrometry, MALDI mass spectrometry and combinations thereof.

29. (Previously presented) A method according to claim 21, wherein prior to said proteolyzing step (c), said one or more active target proteins bound to said probe are bound to a solid support.

30. (Previously presented) A method according to claim 21, wherein said method further consists essentially of adding one or more standard proteins to said complex protein mixture prior to said proteolysis step (c).

31. (Original) A method according to claim 30, wherein said standard protein(s) are labeled with an activity based probe prior to addition to said complex protein mixture.

32. (Previously presented) A method according to claim 31, wherein said standard protein(s) are labeled with an activity based probe consisting essentially of a functional group, a detectable label, an optional affinity group, and an optional linking group, wherein said detectable label is distinguishable from said activity based probe contacted with complex protein mixture.

33 – 47. (Cancelled)

48. (Previously presented) A method according to claim 21, wherein said complex protein mixture is a proteome.

49. (Previously presented) A method for determining the presence, amount, or activity of one or more active target proteins in a complex protein mixture, the method comprising:

(a) contacting said complex protein mixture with a single activity based probe that specifically binds predominantly to a single target site on one or more active target proteins, wherein said probe comprises a fluorescent moiety;

(b) proteolyzing said active target protein(s) to produce a product mixture;

(c) separating said product mixture into two or more components, one or more of which comprise peptides bound to said probe, said probe using a receptor that specifically binds to said probe, wherein said receptor is an antibody or fragment thereof that binds to said fluorescent moiety; and

(d) generating a signal from said peptides bound to said probe, wherein said signal is correlated to the presence, amount, or activity of said one or more active target proteins in said complex protein mixture.

50. (Previously presented) A method according to claim 49, wherein said signal is a fluorescent signal generated from said probe.

51. (Previously presented) A method according to claim 49, wherein said signal is a mass spectrum.

52. (Previously presented) A method according to claim 49, wherein, prior to said proteolyzing step (b), one or more components of said complex protein mixture not bound to said probe are removed from said complex protein mixture.

53. (Previously presented) A method according to claim 49, wherein said probe comprises a label selected from the group consisting of the fluorescent moiety and an isotopic label.

54. (Previously presented) A method according to claim 49, wherein said separating step (c) comprises one or more separation methods selected from the group consisting of affinity separation, gel electrophoresis, capillary electrophoresis, liquid chromatography, HPLC, electrospray ionization mass spectrometry and MALDI mass spectrometry.

55. (Previously presented) A method according to claim 49, wherein prior to said proteolyzing step (b), said one or more active target proteins bound to said probe are bound to a solid support.

56. (Previously presented) A method according to claim 49, wherein said method further comprises adding one or more standard proteins to said complex protein mixture prior to said proteolysis step (b).

57. (Previously presented) A method according to claim 56, wherein said standard protein(s) are labeled with an activity based probe prior to addition to said complex protein mixture.

58. (Previously presented) A method according to claim 57, wherein said standard protein(s) are labeled with an activity based probe comprising the fluorescent moiety that is distinguishable from said activity based probe contacted with complex protein mixture.

59. (Previously presented) A method according to claim 49, wherein said complex protein mixture is a proteome.

60. (Withdrawn) A method for comparing the presence, amount or activity of one or more active target proteins in each of two or more discrete proteomes, the method comprising:

(a) contacting each of said discrete proteomes with a single activity based probe that binds predominantly to a single target site on one or more active target proteins, wherein the same activity based probe is used for each discrete proteome;

(b) proteolyzing said discrete proteomes to produce a product mixture;

(c) separating each of said product mixtures into two or more components, one or more of which comprise peptides bound to said probe; and

(d) comparing the presence, amount or activity of the active target proteins in each of the discrete proteomes by generating a signal from said one or more components comprising peptides bound to said probe.

61. (Withdrawn) The method according to claim 60 wherein said activity based probe binds specifically to a single target site on one or more active target proteins.

62. (Withdrawn) The method according to claim 60 wherein said activity based probe covalently binds to a single target site on one or more active target proteins.

63. (Withdrawn) A method according to claim 60, wherein said separating step (c) comprises sequestering one or more peptides bound to said probe using a receptor that specifically binds to said probe.

64. (Withdrawn) A method according to claim 63, wherein said probe comprises a fluorescent moiety, and said receptor is an antibody or fragment thereof that binds to said fluorescent moiety.

65. (Withdrawn) A method according to claim 60, wherein said probe comprises a fluorescent moiety, and said signal is a fluorescent signal generated from said probe.

66. (Withdrawn) A method according to claim 60, wherein said signal is a mass spectrum.

67. (Withdrawn) A method according to claim 60, wherein, prior to said proteolyzing step (b), one or more components of said complex protein mixture not bound to said probe are removed from said complex protein mixture.

68. (Withdrawn) A method according to claim 60, wherein said probe comprises a label selected from the group consisting of a fluorescent moiety and a biotin moiety.

69. (Withdrawn) A method according to claim 60, wherein said separating step (c) comprises one or more separation methods selected from the group consisting of affinity separation, gel electrophoresis, capillary electrophoresis, liquid chromatography, HPLC, electrospray ionization mass spectrometry, MALDI mass spectrometry and combinations thereof.

70. (Withdrawn) A method according to claim 60, wherein prior to said proteolyzing step (b), said one or more active target proteins bound to said probe are bound to a solid support.

71. (Withdrawn) A method according to claim 60, wherein said method further comprises adding one or more standard proteins to said complex proteome mixture prior to said proteolysis step (b).

72. (Withdrawn) A method according to claim 71, wherein said standard protein(s) are labeled with an activity based probe prior to addition to said complex protein mixture.

73. (Withdrawn) A method according to claim 72, wherein said activity based probe labeling said standard proteins comprises a fluorescent moiety that is distinguishable from said activity based probe contacted with complex protein mixture.

74. (Previously presented) A method for detecting the presence, amount or activity of one or more active target proteins in a single complex protein mixture, the method comprising:

(a) contacting said complex protein mixture with an activity based probe that specifically binds predominantly to a single target site on one or more active target protein;

(b) proteolyzing said active target proteins to produce a product mixture;

(c) separating said product mixture into two or more components, one or more of which comprise peptides bound to said probe; and

(d) generating a signal from said peptides bound to said probe, wherein the signal is correlated to the presence, amount, or activity of said one or more active target proteins in said complex protein mixture.